

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Joacim Elmen et al. Art Unit : 1635  
Serial No. : 10/550,152 Examiner : Tracey Ann Vylemore  
Filed : January 4, 2007 Conf. No. : 1052  
Title : SHORT INTERFERING RNA (SiRNA) ANALOGUES

**MAIL STOP AMENDMENT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**DECLARATION BY JOACIM ELMEN UNDER 1.131**

I, Joacim Elmen, a citizen of Sweden, residing in Malmö, Sweden, hereby declare as follows:

1. I am an inventor of the subject matter disclosed and claimed in the above-referenced patent application.
2. I am familiar with the present claims of the above-referenced patent application, which are directed to:
3. Prior to July 26, 2002, the inventors had conceived the invention as described and claimed in the above-identified application in a WTO country, as evidenced below, by designing double stranded compounds comprising at least one locked nucleic acid (LNA) according to the compound described in present claim 67 of the above-references application. The compounds were synthesized by routine automated oligonucleotide synthesis by Cureon A/S, now known as Santaris Pharma A/S.
4. Attached as Exhibit 1 is a true and accurate copy of oligonucleotide order forms, with dates redacted, showing that certain oligonucleotides comprising at least one LNA were designed prior to July 26, 2002. Exhibit 1 illustrates the design of six single-stranded oligonucleotides, 2184, 2185, 2186, 2187, 2188 and 2189 corresponding to the first eight compounds listed in Table 1 of the above-captioned application. As in Table 1 of the above-captioned application, the order form uses uppercase letters in the oligonucleotide designs to represent a beta-D-oxy LNA monomer, as further illustrated by the superscript "o" immediately subsequent to each

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uppercase letter. Like Table 1, the order form uses lowercase letters to represent an RNA monomer, as illustrated by the subscript "r" preceding each lowercase letter in the oligonucleotides. These oligonucleotides, which target the Firefly luciferase, were designed to form double stranded compounds comprising a sense strand and an antisense strand, as specified in presently pending claim 67. Certain of the double-stranded compounds were used in Examples 6 - 8 (Figures 2-6) of the above-captioned application.

In sum, I submit evidence herewith that shows conception and reduction to practice of the claimed invention prior to July 26, 2002.

6. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, under Title 18 § 1001 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

22/11-10

Date

Joacim Elmén

J

SPC no.: SPC-02184-01

Project: Cureon

Ordered by: hfh

Order date: [REDACTED] 15:28:58

5'- rC rU rU rA rC rG rC rU rG rA rG rU rA rC rU rU rC rG rA T<sup>o</sup> T<sup>o</sup> -3'

Mw (cal): 6443.15 $\mu$ g

Extinction coefficient: 200.9

1 Od 260 = 4.98 $\mu$ M

Mw (meas): 0

Concentration:

Volumen:

Synthesis scale: 1

Purification: none

Priority: N

Synth. by:

Synth. start date: [REDACTED]

Synth. end date: [REDACTED]

RNAi C. Wahlstedt

Synthesis was performed the [REDACTED]

This oligo was approved and released the [REDACTED]

The oligo was sent to Claes Wahlestedt the [REDACTED]

AMS

Synthesis comments:

SPC no.: SPC-02185-01

Project: Cureon

Ordered by: hfh

Order date: [REDACTED] 15:30:01

5'- mC<sup>o</sup> rU rU rA rC rG rC rU rG rA rG rU rA rC rU rU rC rG rA T<sup>o</sup> T<sup>o</sup> -3'

Mw (cal): 6485.19 $\mu$ g

Extinction coefficient: 199.9

1 Od 260 = 5 $\mu$ M

Mw (meas): 0

Concentration:

Volumen:

Synthesis scale: 1

Purification: none

Priority: N

Synth. by:

Synth. start date: [REDACTED]

Synth. end date: [REDACTED]

RNAi C. Wahlstedt

Synthesis was performed the [REDACTED]

This oligo was approved and released the [REDACTED]

The oligo was sent to Claes Wahlestedt the [REDACTED]

AMS

Synthesis comments:

SPC no.: SPC-02186-01

Project: Cureon

Ordered by: hfh

Order date: [REDACTED] 15:32:30

5'- rU rC rG rA rA rG rU rA rC rU rC rA rG rC rG rU rA rA rG T<sup>o</sup> T<sup>o</sup> -3'

Mw (cal): 6501.22 $\mu$ g

Extinction coefficient: 211.9

1 Od 260 = 4.72 $\mu$ M

Mw (meas): 0

Concentration:

Volumen:

Synthesis scale: 1

Purification: none

Priority: N

Synth. by:

Synth. start date: [REDACTED]

Synth. end date: [REDACTED]

RNAi C. Wahlstedt

Synthesis was performed the [REDACTED].

This oligo was approved and released the [REDACTED]

The oligo was sent to Claes Wahlestedt the [REDACTED]

AMS

Synthesis comments:

SPC no.: SPC-02187-01

Project: Cureon

Ordered by: hfh

Order date: [REDACTED] 15:34:15

5'- T<sup>0</sup> rC rG rA rA rG rU rA rC rU rC rA rG rC rG rU rA rA rG T<sup>0</sup> T<sup>0</sup> -3'

Mw (cal): 6529.23µg

Extinction coefficient: 210.9

1 Od 260 = 4.74µM

Mw (meas): 0

Concentration:

Volumen:

Synthesis scale: 1

Purification: none

Priority: N

Synth. by:

Synth. start date: [REDACTED]

Synth. end date: [REDACTED]

RNAi C. Wahlstedt

Synthesis was performed the [REDACTED]

This oligo was approved and released the [REDACTED]

The oligo was sent to Claes Wahlestedt the [REDACTED]

AMS

Synthesis comments:

SPC no.: SPC-02188-01

Project: Cureon

Ordered by: hfh

Order date: [REDACTED] 15:36:53

5'- C<sup>o</sup> T<sup>o</sup> T<sup>o</sup> rC rg rC T<sup>o</sup> ra rg T<sup>o</sup> ra rC T<sup>o</sup> T<sup>o</sup> rC rg ra T<sup>o</sup> T<sup>o</sup> -3'

Mw (cal): 5996.81 $\mu$ g

Extinction coefficient: 171.8

1 Od 260 = 5.82 $\mu$ M

Mw (meas): 0

Concentration:

Volumen:

Synthesis scale: 1

Purification: none

Priority: N

Synth. by:

Synth. start date: [REDACTED]

Synth. end date: [REDACTED]

RNAi C. Wahlstedt

Synthesis was performed the [REDACTED]

This oligo was approved and released the [REDACTED]

The oligo was sent to Claes Wahlestedt the [REDACTED]

AMS

Synthesis comments:

SPC no.: SPC-02189-01

Project: Cureon

Ordered by: hfh

Order date: [REDACTED] 15:39:08

5'- T<sup>0</sup> rC rg ra ra rg T<sup>0</sup> ra rC T<sup>0</sup> rC ra rg rc rg T<sup>0</sup> ra ra rg T<sup>0</sup> T<sup>0</sup> -3'

Mw (cal): 6613.26 $\mu$ g

Extinction coefficient: 207.7

1 Od 260 = 4.81 $\mu$ M

Mw (meas): 0

Concentration:

Volumen:

Synthesis scale: 1

Purification: none

Priority: N

Synth. by:

Synth. start date: [REDACTED]

Synth. end date: [REDACTED]

RNAi C. Wahlstedt

Synthesis was performed the [REDACTED]

This oligo was approved and released the [REDACTED]

The oligo was sent to Claes Wahlestedt the [REDACTED]

AMS

Synthesis comments: